SUPPORT FOR THE AMENDMENTS

The present amendment cancels claims 1-20 and 32-53, amends claim 21, and adds new claims 54-56.

Support for newly added claims 54-56 is found in the originally filed claims (See e.g., claims 1 and 2) and specification (See e.g., page 4, lines 1-4).

It is believed that these amendments have not resulted in the introduction of new matter.

REMARKS

Claims 21-31 and 54-56 are currently pending in the present application. Claims 1-20 and 32-53 have been cancelled, claim 21 has been amended, and new claims 54-56 have been added, by the present amendment.

The rejection of claims 32-42 under 35 U.S.C. § 103(a) as being obvious over Sarkar (Journal of Biological Chemistry) in view of Endo (U.S. Patent 5,569,464) is moot in view of the cancellation of said claims.

The rejection of claims 43-53 under 35 U.S.C. § 103(a) as being obvious over Akimoto (U.S. Patent 5,849,716) in view of Endo is moot in view of the cancellation of said claims.

The rejection of claims 5-31 under 35 U.S.C. § 103(a) as being obvious over either Izumi (JP 11-060592) or Shin (JP 00-191685) in view of Endo is obviated by amendment in part, with respect to the cancellation of claims 5-20, and is respectfully traversed in part, with respect to claims 21-31 and newly added claims 54-56.

Claim 21 recites, in part, a liposomal composition comprising a cholestanyl glycoside according to formula (1), which has a sugar moiety selected from the group consisting of GlcNAc-Gal-, GlcNAc-Gal-Glc-, and Fuc-Gal- and exhibits antitumor activity, and a phospholipid and a positive-charge-providing substance capable of forming a liposome. Applicants have surprisingly discovered that the liposomal composition comprising the cholestanyl glycoside of the present invention unexpectedly exhibits a remarkable degree of enhanced anti-tumor efficacy.

Izumi describes an anticancer medicine comprising a cholestanyl glycoside having a Fuc-Gal- sugar moiety (See e.g., abstract). In contrast to the presently claimed invention, Izumi fails to disclose or suggest incorporating the cholestanyl Fuc-Gal- glycoside into a

liposomal composition, which further comprises a phospholipid and a positive-charge-providing substance.

Shin describes an anticancer agent comprising a cholestanyl glycoside having a GlcNAc-Gal- sugar moiety (See e.g., abstract). In contrast to the presently claimed invention, Shin fails to disclose or suggest incorporating the cholestanyl GlcNAc-Gal-glycoside into a liposomal composition, which further comprises a phospholipid and a positive-charge-providing substance.

Endo describes incorporating hydrophilic or lipophilic active agents into a liposomal composition comprising a phospholipid (e.g., dipalmitoylphosphatidylcholine) and a positive-charge-providing substance (e.g., an aliphatic amine, such as stearylamine) (See e.g., column 2, lines 37-40 and 49-50, column 3, lines 57-59 and 64-65) for the purpose of controlled and targeted release of the active agents, as well as the stabilization of unstable active agents (See e.g., column 1, lines 20-24). The carcinostatic agents include antitumor antibiotics (i.e., mitomycin, doxorubicin or adriamycin), antimetabolites (i.e., methotrexate and tegafur), a platinum compound (i.e., cisplatin), and a vinca alkaloid (i.e., vincristine) (See e.g., column 4, lines 51-52).

Endo fails to provide sufficient motivation and guidance to direct a skilled artisan to particularly select the claimed cholestanyl glycoside anticancer agents from either the tremendously broad genus of hydrophilic or lipophilic active agents, or the preferred carcinostatic agents described therein.

Even if sufficient motivation and guidance is considered to have been provided by Endo to direct a skilled artisan to particularly select the cholestanyl Fuc-Gal- glycoside anticancer medicine of Izumi and/or the cholestanyl GlcNAc-Gal- glycoside anticancer agent of Shin for incorporation into the liposomal composition of Endo, such a case of obviousness

is rebutted by a showing of unexpected results, as shown by the experimental data presented in Figures 1 and 2 of the present specification.

A general increase in antitumor efficacy attributable to incorporating cholestanyl anticancer agents into a liposomal composition may be reasonably expected, due to the stabilization and controlled/targeted delivery thereof (See e.g., "Chol" and "Chol-Lipo" illustrated in Figures 1 and 2). However, the presently claimed cholestanyl glycoside anticancer agents *surprisingly exhibit drastically enhanced antitumor efficacy far beyond that which may be reasonably expected* by the incorporation of the cholestanyl glycoside anticancer agents into a liposomal composition (See e.g., "GlcNAcβ1,4GalChol" and "GlcNAcβ1,4GalChol-Lipo" illustrated in Figure 1, and "Fucα1,3GalChol" and "Fucα1,3GalChol-Lipo" illustrated in Figure 2). That is, while a skilled artisan may have reasonably expected an enhancement in antitumor efficacy by incorporating the cholestanol glycoside anticancer agents into a liposomal composition, due to the stabilization and controlled/targeted delivery thereof, the *remarkable degree of enhanced anti-tumor efficacy*, as evidenced in Figures 1 and 2, *was quite unexpected.*

While wishing not to be bound to any particular theory, Applicants believe that the cholesterol aglycone (nonsugar component) of the claimed cholestanyl glycoside anticancer agents possesses affinity for, and is thus incorporated into, the liposomal membrane, whereby the sugar moiety is orientated on the surface of the liposome, thereby surprisingly exhibiting a remarkable degree of enhanced antitumor efficacy.

Withdrawal of this ground of rejection is respectfully requested.

In conclusion, Applicants submit that the present application is now in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

David P. Stitzel
Attorney of Record
Registration No. 44,360

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 06/04)